Effect of Traditional Herbal Medicine Therapy on Menometrorrhagia: Case Report

Mejda Selmi[1, 2]Zarkalai Feten[4], Latifa Lassoued[1, 3]Badra Bannour[1, 3]Ridha Charfeddine[5], Hedi khairi[1, 3]

[1]Université de Sousse, Faculté of Médicine de Sousse, 4000, Sousse, Tunisie.
[2]Laboratoire de recherche de biophysique métabolique ET pharmacologie appliquée (LR12ES02), 4000, Sousse, Tunisie
[3]Hopital Farhat Hached, Service de Gynécologie Obstétrique, 4000. Sousse, Tunisie
[4]Laboratory of Adaptation of Plants to Abiotic Stress, Borj Cedria Biotechnology Center, Borj-Cedria Technopole (CBBC), Hammam-Lif, Tunis.
[5]UNIMED laboratories, Industrial Zone Kalaa Kebira, BP 38 Sousse 4060, Tunisia,
∗Correspondence should be addressed to: Mejda Selmi
E-mail: mejda.selmi@gmail.com

Abstract.
Background: Surgical intervention seems to be the only procedure in the management of uterine fibroids symptoms, having numerous sequelae in women's general health. Methods: 45-year-old woman, single, with a medical history of thyroidectomy and myomectomy. She presented with critical anemia in hemoglobin 4 g/dt and complaints of prolonged, excessive, and irregular uterine bleeding. Pelvic ultrasound showed multiple uterine fibromas with the largest one measuring 5 cm in diameter and intra-cavitary fibroid (FIGO 0) measuring 3.5 cm. She was unresponsive to drug treatment and hysterectomy was recommended but the patient refused. Given her serious health condition, she was given a mixture of two medicinal plants, taken as tea infusion by the oral route for three consecutive days during three consecutive months. Results: A decline in the mean number of bleeding days was noted. The bleeding intensity score declined from 102 (±15.3) to 75 (± 12.3), and regularization in menstrual cycle was also noted. Thus, the surgical procedure was avoided in the present case. Conclusion: This study explored a new approach to treat menometrorrhagia based on tea infusion consumption. It also paved the way for future studies to further investigate critical cases of uterine fibroma.
Keywords: Meno-metrorrhagia, Hysterectomy, Traditional herbal Medicine, Uterine fibroids

1. Introduction

Menometrorrhagia is excessive uterine bleeding resulting from a combination of two different conditions, namely menorrhagia, which is heavy bleeding during the menstrual period, [1] and metrorrhagia, when the period lasts more than seven days or when uterine bleeding exists between periods [2]. Is a worldwide health problem affecting 20% of adolescent girls and more than 50% of women older than 45 years [3]. Surgical treatment becomes a necessity after the failure of a medical treatment [3] Hysterectomy represents the main treatment option for uterine myoma. It is a major surgical procedure having numerous sequelae in women's general health [4] It also interferes with women's physical, social, emotional, and material quality of life. Because of these serious side effects, it is therefore logical to investigate other available sources to look for an efficacious treatment to manage the symptoms caused by this disease. Such problems may be beyond the scope of herbal treatment. *Mentha pulegium,* commonly known as *Pennyroyal,* and *Artemisia abrotanum L*, commonly known as *Southernwood*, are largely used in the Tunisian traditional remedies. These two herbs are known to stimulate uterus muscle during painful or strong menstruation [5]. They are also considered as a foodstuff by the European Herbal Infusions Association and are used in pharmaceutical and agro-alimentary industries [6]. This work presents the clinical manifestation and the beneficial effects of the tea infusion of a combination of these two herbal medicines in the treatment of patients with menometrrorhagia that is unresponsive to medication.

2. Case presentation

We, herein, report a case involving a 45-year-old female patient, single, G0P0, of 165cm in height and 88 kg in weight, with a past medical history of subtotal thyroidectomy. Her very first presentation had been to the Emergency department in 2014 with excessive persistent vaginal bleeding and critically low hemoglobin (Hb) (4 g/dl). Investigations, including ultrasound showed fibroid uterus. Urgent myomectomy had therefore been performed with blood transfusion. She had been discharged after few days of hospitalization with Norethisterone and ferrous sulphate treatment.

In October 2019, she presented to the Emergency department of Gynecology and obstetrics at Farhat Hached University Hospital, Sousse, Tunisia, with a recurrence of prolonged and excessive vaginal bleeding for more than 15 days. She had anemia with hemoglobin level of 6.2 g/dl. At her initial evaluation, magnetic resonance imaging(MRI) showed an increased uterus size with irregular borders and multiple uterine fibromas, mainly in the submucosal, subserosal, and intra-cavitary areas, with the largest one measuring 5 cm in diameter located in the posterior fundus with an intra-cavitary fibroid (FIGO 0) measuring 3.5 cm (figure 2). Diagnosis of menometrorrhagia was therefore made. Hysterectomy was recommended but the patient

doi.org/10.31838/hiv22.02.218 Received: 25.06.22, Revised: 26.06.22, Accepted: 24.08.22

refused to undergone this surgical procedure. She received blood transfusion and her symptoms were managed medically. On discharge, Norethisterone and ferrous sulfate tablets were prescribed for four months. The patient continued to have heavy prolonged bleeding, pain, and clot secretion. Initial vital signs revealed a temperature of 36.3 °C, blood pressure of 150/90 mm Hg, and heart rate of 100 beats/min. Initial laboratory results showed low hemoglobin of 6.3g/dl. The patient received blood transfusions and intravenous iron. She was discharged with hemoglobin of 8.7g/dl. Again, the patient refused to undergo hysterectomy. Given her serious health condition, we proposed to test the effect of herbal tea infusion of a mixture of two medicinal plants, traditionally known by their hemostatic effect. The plants were tested and studied for security and tolerability for administration. Details of the herbs are presented in (Table 3).

Intervention

The treatment consists of the crushed leaves of the two plants without any other additive. Herbal tea infusion was taken by the patients at home after providing her with detailed oral and written explanation. The herbs were taken as tea infusion through the oral route. Five g of dried aerial parts of a combination of the two plants were added to 100 ml of boiling water and infused for 10 to 15 min. The tea infusion was taken through the oral route before food three times a day at 4-hour intervals starting from the onset of menstruation for three consecutive days during three consecutive months.

Follow-up

The patient was followed via phone calls during and after the treatment. She was followed-up for three months. Monitoring for efficacy and safety was performed every month starting from the treatment initiation until the treatment completion (table 1)

Outcomes

Disappearance of pain and blood clotting was noted, with improvement in blood count, and bleeding duration and intensity (Table 1). The patient returned to her normal life with seven days of menstrual bleeding and 75 score of pictorial chart. The long-term effect of the tea infusion of the herbal treatment was noted from September 2020 until June 2022. The tolerability of mixed Pennyroyal and Southernwood with regard to biochemical parameters before the onset of the treatment and after three months was in the normal range (Table 2). The tea infusion consumed was well-tolerated and the patient did not report any serious adverse events. *Pennyroyal* and *Southernwood* have an interesting antioxidant activity and an important polyphenol and flavonoids amount (Table 3).

Both plants showed a value of nitrate and nitrite under 0.1 mg/kg. As for the cyanide level, it was 2.26 ± 0.07mg/kg in Pennyroyal and 1.93 ±0.06 mg/kg in Southernwood.

3. Discussion

Menometrorrhagia is a frequent cause of medical consultations. It consists of menorrhagia, which is excessive menstrual flow, and metrorrhagia, known as irregular and prolonged duration of bleeding [7]. It is occasionally caused by uterine myomas. It is responsible for abdominal distension, pain, and urinary symptoms. It may also cause heavy and prolonged menstrual bleeding, which can lead to iron-deficiency, anemia, and social embarrassment [8]. According to Robert et al. [5] the treatment decision depends on the nature of the lesion to be treated.When organic uterine lesions are present, several medical treatments, such as anti-fibrinolytic agents, nonsteroidal anti-inflammatory drugs, progestin, oral contraceptive pills, GnRH agonists, and danazol are efficient. They act by suppressing the cause of bleeding or by their symptomatic action [6]. Surgical treatment is necessary after the failure of medical treatments or in the presence of a lesion that is not directly accessible to medical therapy [3]. The surgical procedure consists of endoscopic techniques (operative hysteroscopy and laparoscopy) [3]. Hysterectomy represents the main treatment option for uterine myoma. It is a major surgical procedure having numerous sequelae in women's general health [3]. It interferes with women's physical, social, emotional, and material quality of life [9] Our results were consistent with those of Thubert et al. [9]. showing that *Pennyroyal* is effective in reducing the number of days of menstrual flow and in normalizing the cycle in patients with infrequent periods of more than 35 days or with scanty flow, both in amount and duration [9]. This tea infusion combination of the two plants and the general improvement in the patient's quality of life may have been due to the synergy for the mixtures of the phytochemicals of both plants. Through this study results, *Pennyroyal* and *Southernwood* have significant potential to inhibit free radical activity therefore reducing oxidative damage. A study performed by Baiceanu et al. [10]. Showed that the high active compounds of chemical compositions of aqueous extract of *Southernwood* are sinapic acid, ferulic acid, luteolin, rutin, and patuletin [10]. These five major compounds are known in literature with their potential anti-inflammatory and antioxidants activity [11]. However, polyphenols and flavonoids have been the focus of much early research for their antioxidant properties that could contribute to their observed anti-inflammatory and anti-platelet effects [12]. which probably confirms the traditional use of a combination of these two herbs for women during menstruation or for their hemostatic properties The obtained results showed that the aerial parts of *Pennyroyal* and *Southernwood* are safe for consumption, with nitrite and nitrate amounts being under permissible levels in both herbs [13]. Study mad by Pinela et al on toxicity of chemicals in food [14] suggest that humans are sensitive to cyanide toxicity, since the lethal dose ranges from 3.5 mg/kg [14]. Therefore, our results showed that cyanide concentration in the powder of the aerial parts of both herbs was lower than the toxic level.

4. Conclusion

The results of this case report showed the possible effect of this herbal treatment in the management of patients with menometrorrhagia that is unresponsive to medical treatment. The tea infusion of a mixture of the two plants may improve the clinical curative effect of menometrorrhagia, thus providing a new way that may help to avoid the surgical procedure and to improve women's quality of life. This case report paves the way for a pre-clinical study involving a placebo group to investigate the effect of herbal tea infusion on a large scale.

Abbreviations

CBC: Complete blood count, Hbg: Hemoglobin, Hct : Hematocrit, MCV : Mean corpuscular Volume, MCH: Mean corpuscular haemoglobin, PLT: Platelet count, PT : Prothrombin Time
INR: Prothrombin Rati, Fib: Fibrinogen, AUB: Abnormal Uterine Bleeding

5. Acknowledgements

Authors would like to thinks the women of this case repot and express their grateful to Mr Samir Boukhattaia for proof reading this work.

Author's contribution

Mejda selmi and Zarkalai Feten and Hedi khairi are responsible for development of the study. Mejda Selmi and Latifa Lassoued contributed to data analysis and interpretation. Mejda Selmi and Badra Bannour and Hedi Khairi contributed to writing the article or critical analysis leading to significant changes to the intellectual content. Mejda Selmi, Zarkalai Feten, Latifa Lassoued. Badra Bannour, Hedi Khairi contributed to final approval of the version submitted after critical review.

Funding

This work was not supported by any grants.
Availability of data and materials
All data used during the present study are available from the corresponding
Author on reasonable request.
Ethics approval and consent to participate
This case report was ethically approved by the Human Research Ethics committee at the Faculty of Medicine of Sousse,
Consent for publication
Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.
Competing interests

Table 1. Results of laboratory test, menstrual bleeding PBAC Score bleeding amount before and after herbal treatment

Parameters	Before herbal treatment (mean of three months)	After herbal treatment (mean of three months follow-up)	P-value	Reference VALUE
RBC	2.76 (± 0.73)	4.3 (± 0.34)	1.21	(4.2-5.4)
Hbg g/dl	6.23 (± 2.35)	13.0 (± 0.7)	0.05	(12-16)
Hct %	23.46 (± 6.89)	38.72 (± 1.67)	0.08	(37-46)
MCV fl	82.16 (± 7.07)	90 (± 4.36)	0.07	(80-96)
MCH pg	24,86 (± 3.66)	31,83 (± 2.01)	0.15	(28-32)
PLT *103/l	110 (± 60.6)	208,8 (± 19 .7)	0.64	(150-450)
Menstrual bleeding duration (days)	17.6 (± 2.5)	7.3 (± 1)	0.73	(7 – 10)
*Score of PBAC bleeding amount	102.6	75.3	0.62	<100

CBC : Complete blood count, Hbg : Hemoglobin, Hct : Hematocrit, MCV : Mean corpuscular Volume, MCHC: Mean corpuscular haemoglobin concentration, PLT: Platelet count,
Data are expressed as mean ± standard deviation
P< 0.05
*PBAC : Pictorial blood loss assessment charts, to diagnose heavy menstrual bleeding : score of the sum

Table 2: Change in biochemical parameters before and after the herbal treatment

	Before	After (days 91)	
Direct Bilirubin (mg/L)	1.47	1.97	< 3
Total Bilirubin (mg/L)	5.32	5.84	< 12
(LDH) Lactate dehydrogenase (UI/L)	241	243	< 480
Glycemia a(mmol /L)	5.66	5.61	(3.9 - 6.1)
Creatinie (µmol/L)	63,74	57.74	(53.04 - 119.34)
Urea (mmol /L)	4.53	3.67	(2.94 – 7.47)
Fibrinogen g/l	5.4	3,7	(2-4)
Prothrombin Time (PT) (%)	96	100	(70-100)
Prothrombin ratio (INR)	0.7	1.3	(1 - 1.3)

Table 3. Total polyphenol and flavonoïds compounds, anti-nutriments and antioxidant activity contents in the aerial parts of Tunisian Mentha Pulegium L and Artemisia Abrotanum L

Plants	Total polyphenol content (mg GAE g−1 DW) Mean±SD	Total Flavonoid content (mg CE g−1 DW) Mean±SD	*Anti-nutriments mg/kg		Antioxidant activity IC50% (µg/mL)	
			Nitrates	Nitrites	Cyanides	

Pennyroyal	22.580 (±1.31)	9.685 (±0.80)	<0.1	<0.1	2.33	54.45 (±25.53)
Southernwood	11.601 (±0.35)	5.727 (±0.15)	<0.1	<0.1	1.99	60.61 (±±19.71)

-Means :three replicates; mg GAE g −1 DW: milligrams gallic acid equivalent per gram dry weight; mg CE g−1 DW: milligrams catechin equivalent per gram dry weight.
Antioxidant activity of two methanolic extract concentrations in the aerial parts of Pennyroyal and Southernwood using the 2,2-Diphenyl-1-picrylhydrazyl (DPPH) Radical Scavenging Method
* Nitrates and Nitrates, were determined, according to the (AFNOR ISO 7890-3) and (AFNOR ISO 6777) respectively, and Cyanides was determined according to the photometry method WTW 250344 using HPLC Agilent 1200.
Mentha pulegium L: Pennyroyal
Artemisia abrotanum L: Southernwood

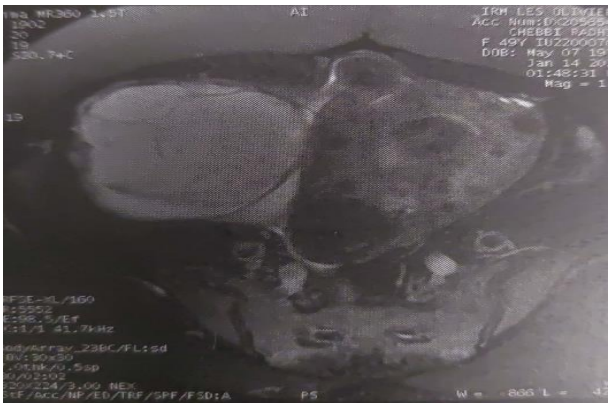

Figure 2: MRI photo of fibromas intr-acavitary area measuring 5 cm of diameter located in the posterior fundus with intra-cavitary fibroids (FIGO 0) measuring 3.5 cm.

Reference

1Fathima A, Sultana A. Clinical efficacy of a Unani formulation 'Safoof Habis' in menorrhagia: A randomized controlled trial. European Journal of Integrative Medicine. 2012;4(3):e315-e22. https://doi.org/10.1016/j.eujim.2012.01.007

2.Fritz MA, Speroff L. Endometriosis in Clinical Gynecologic Endocrinology and Infertility. 8th eds. Lippincott Williams and Wilkins. Philadelphia; 2011.

3.Donnez J. Menometrorrhagia during the premenopause: an overview (vol 27, pg 1114, 2011). GYNECOLOGICAL ENDOCRINOLOGY. 2012;28(2):156-.

4.Donnez J, Dolmans M-M. Uterine fibroid management: from the present to the future. Human reproduction update. 2016;22(6):665-86. https://doi.org/10.1093/humupd/dmw023

5.Robert Y, Bazot M. Imagerie des méno-métrorragies. Journal de radiologie. 2008;89(1):115-32. https://doi.org/10.1016/S0221-0363(08)70383-4

6.Moroni R, Vieira C, Ferriani R, Candido-dos-Reis F, Brito L. Pharmacological treatment of uterine fibroids. Annals of medical and health sciences research. 2014;4(3):185-92. https://doi.org/10.4103/2141-9248.141955

7.Fraser IS, Critchley H, Munro M, Broder M. Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding? Human reproduction. 2007;22(3):635-43. https://doi.org/10.1093/humrep/del478

8.Firdose K, Begum W, Shameem I, Jahan M, Firdose N. Clinical Evalution of Qillat Tams and its Management with Unani Formulation. International Research Journal of Medical Sciences. 2013;1(11):1-8. . Available from: https://www.researchgate.net/publication/329539582

9.Thubert T, Demoulin G, Lamazou F, Rivain A-L, Trichot C, Faivre E, Deffieux X. Menometrorrhagia. La Revue du praticien. 2014;64(4):531-9. https://doi.org/10.3109/09513590.2012.637341.

10.Baiceanu E, Vlase L, Baiceanu A, Nanes M, Rusu D, Crisan G. New polyphenols identified in Artemisiae abrotani herba extract. Molecules. 2015;20(6):11063-75. https://doi.org/10.3390/molecules200611063

11.Chen C. Sinapic acid and its derivatives as medicine in oxidative stress-induced diseases and aging. Oxidative medicine and cellular longevity. 2016;2016. https://doi.org/10.1155/2016/3571614

12.Robak J, Gryglewski R. Bioactivity of flavonoids. Polish journal of pharmacology. 1996;48(6):555-64. Available from: https://europepmc.org/article/med/9112694

13.Meeting JFWECoFA, Additives JFWECoF, Organization WH. Evaluation of Certain Food Additives and Contaminants: Sixty-first Report of the Joint FAO/WHO Expert Committee on Food Additives. World Health Organization, 2004. Available from: https://books.google.com.pk/books?id=K7OaG7wzwtAC

14.Pinela J, Carvalho AM, Ferreira IC. Wild edible plants: Nutritional and toxicological characteristics, retrieval strategies and importance for today's society. Food and Chemical Toxicology. 2017;110:165-88. https://doi.org/10.1016/j.fct.2017.10.020